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Risk Factors for Prevalent Human Immunodeficiency Virus (HIV) Infection in Active Duty Army Men Who Initially Report No Identified Risk: A Case-Control Study

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Summary: A large proportion of human immunodeficiency virus antibody (HIV-Ab) positive male soldiers are considered to be at no identified risk (NIR) because they do not disclose histories of sexual activity with other men, intravenous drug use, blood transfusions, or sexual activity with persons at known high risk for HIV infection. A case-control study involving personal interviews with 26 NIR cases and 74 controls was conducted to determine if lifestyle information that might jeopardize a soldier's military career could be obtained from an Army population and to evaluate risk factors for prevalent HIV infection. Subjects consented to a voluntary, anonymous, and confidential interview containing information on demographic characteristics, medical history, drug use, and sexual behavior. Of 26 cases interviewed, 20 (76.9%) reported behaviors defined by the Centers for Disease Control (CDC) as risk factors for HIV infection, while 11 of 74 (14.9%) controls also reported such behaviors. This proportion of reclassified NIR cases was similar to that reported from the NIR case series study conducted by the CDC. Of the six (23.1%) cases who remained at NIR, all reported at least one of the following risks: a history of sexually transmitted diseases, sexual contact with prostitutes, or sexual activity with female partners which caused bleeding. Based on the multivariate analysis, significant or marginally significant independent risks of HIV infection, controlling for age, length of military service, and race were found among men who engaged in sexual activity with male partners [odds ratio (OR) = 21.9, $p = 0.0001$], sexual activity with male or female partners which caused bleeding (OR = 7.3, $p = 0.01$), sexual activity with prostitutes (OR = 3.8, $p = 0.05$), and sexual activity with intravenous drug user (OR = 4.7, $p = 0.06$). These results suggest that study designs that are confidential, anonymous, and blinded can improve the quality of risk factor assessments in individuals who may perceive that divulging such information could be incriminating. **Key Words:** HIV infection—Epidemiology—Risk factors—No identified risk (NIR).



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In October 1985, the Department of Defense instituted a number of routine screening programs for the presence of antibody to human immunodeficiency virus (HIV-Ab) in active duty personnel. Components of the Army HIV Program have been described in detail elsewhere (1-3). Soon after the onset of Army screening programs, preliminary risk factor assessments indicated that infected soldiers often did not report histories of behaviors traditionally associated with an increased risk of HIV infection (i.e., homosexuality, bisexuality, or intravenous drug use). Heterosexual promiscuity, however, particularly involving sex with female prostitutes, was reported as a risk factor among male soldiers (4).

As of July 1989, 1,771 active duty Army individuals have been confirmed to be HIV-Ab positive. The definition of HIV-Ab positivity, screening procedures, and test performance have been reported previously (5-7). All soldiers are personally notified of a positive test by a physician at the post where they are assigned. Subsequent to the initial notification, physicians attempt to ascertain risk factors for infection and to determine if there were high risk contacts, as well as to provide initial counseling and education. HIV-infected soldiers are then referred to one of six Army Medical Centers for comprehensive clinical evaluation. The initial risk assessment interview at the Army post is conducted in private, but follow-up counseling interviews include the HIV-infected soldier's company commander.

Results of initial risk assessment interviews at several posts revealed that approximately 40% of HIV-infected soldiers did not report risks (J. G. McNeil and P. D. Renzullo, unpublished data) as defined by the Centers for Disease Control (CDC) (8). Typically, these soldiers either declined to respond to questions eliciting risk behavior information or they only stated that they had frequently engaged in heterosexual activity that may or may not have included contact with a prostitute. These findings are not unexpected given military regulations that stipulate discharge from the Armed Forces for homosexuality or drug abuse (9).

In order to more rigorously evaluate risk behaviors for HIV infection in this population, we designed a case-control study of HIV infection among active duty male soldiers who were initially classified as having no identified risk (NIR). We thought it was particularly important to determine if we could obtain information on CDC-defined risk be-

haviors for HIV infection from an Army population, especially in a group of soldiers who initially reported no known risk for infection. This report summarizes the results of the pilot investigation.

METHODS

All prevalent cases of HIV infection among active duty male soldiers stationed at one of three Army posts who were identified between October 1985 and October 1987 and who did not initially report a history of CDC-defined risk behaviors for HIV infection were eligible for inclusion in the case group. Cases were defined on the basis of the presence of antibody to HIV (HIV-Ab) using the ELISA test with duplicate Western blot confirmation. Individuals with clinically apparent HIV-related diagnoses were not eligible for inclusion in the study. Controls were randomly selected from the population of all uninfected active duty personnel at each installation where cases were identified. Eligibility for control status required that the soldier tested negative for HIV-Ab no earlier than 3 months before the case to which he was matched. Three controls were matched to each case on age (± 2 years), race/ethnic group (white, non-Hispanic; black, non-Hispanic; Hispanic; Asian; other), rank (junior enlisted, senior enlisted, warrant officer, commissioned officer), and length of military service (± 5 years).

Potential cases were recruited by Community Health Nurses working in the HIV Program at each post. A list of matched controls was generated by investigators at the Walter Reed Army Institute of Research (WRAIR). Participation in the study was strictly voluntary. The study was designed so that investigators could not link risk behavior information to individual subjects, and furthermore, HIV Program personnel working at the posts did not have access to the risk behavior histories obtained during the interview.

Interviews were conducted using a structured questionnaire that sought information on demographic characteristics; medical history, including history of sexually transmitted diseases; intravenous drug use and recreational drug use; sexual behaviors; and other lifestyle behaviors since 1980. In an effort to determine the honesty of responses during the interview, respondents were also asked to complete two self-administered questions. One question asked respondents whether they answered

questions honestly; the second asked whether respondents felt their anonymity would be protected. Interviews lasted approximately 1 h and were conducted by a civilian interviewer from WRAIR. The interviewer was not informed of, and did not solicit during the course of the interview, personal identifiers or HIV-Ab status of any respondent. Of the potential subjects identified for the study, interviews were obtained for 80% of the cases and 85% of the controls.

The measure of association between HIV antibody status and each exposure variable was the odds ratio (OR), with the reference category being men who never had a particular exposure. Initially, univariate estimates of the OR were obtained from fitting an unconditional logistic regression model with the single covariate, adjusted for age (≤ 29 years, > 29 years), length of military service (≤ 5 years, 6–10 years, > 10 years), and race (white, non-white) (10). Multiple logistic regression modeling was used to determine independent risks associated with HIV antibody status. All p values were two-sided and 95% confidence intervals (CI) were calculated using a test-based method (11). Variables entered into the model included sexual activity with male partners, sexual activity with intravenous drug users, sexual activity with male or female partners which caused bleeding, group sex, sexual activity with a prostitute, sexual activity with more than two new partners per year, recreational drug use, and history of sexually transmitted diseases. The final logistic model was determined by using a "step-down" method in which variables were removed one at a time from the full model. A p value less than 0.10 was required to retain a factor in the model. Conditional logistic regression analysis (10), taking into account the matched design of the study, yielded similar results. Unmatched analyses are presented here because they provided more stable estimates of risk.

RESULTS

A total of 26 cases and 74 controls were interviewed at the three Army installations. Respondents were similar by age, length of military service, and race/ethnicity showed that cases and controls were similar on these factors. The mean age was approximately 30 years for both cases and controls. The average length of military service for

cases and controls was 9.8 and 10.5 years, respectively. Among cases, 62% were black, 27% were white, and the remaining 11% were Hispanic or Asian. Among controls, 65% were black, 23% were white, and the remaining 10% were either Hispanic, Asian, or "other."

Ninety-nine percent of the participants reported that they answered questions honestly. The one individual who indicated that he did not answer all questions honestly also did not report engaging in CDC-defined risk behaviors for HIV infection. Seven percent of the participants said they doubted their anonymity would be maintained once the interview was completed. Four of these seven individuals were cases, two of whom did not acknowledge engaging in CDC-defined risk behaviors associated with HIV infection.

Of the 26 NIR cases, 20 (76.9%) reported practicing, since 1980, at least one of the following CDC-defined risk behaviors for HIV infection: sex with a male partner; intravenous drug use; or sex with a female partner who had AIDS, HIV infection, or used intravenous drugs. Of these 20 cases, 14 (70.0%) reported having engaged in sexual activity with male partners; 13 of these 14 cases reported having had sex with both male and female partners, while only 1 case reported sex exclusively with male partners. Three of the 20 cases (15%) reported intravenous drug use since 1980; 2 of these 3 cases also reported having sex with male partners. Finally, nine cases (45%) had sex partners who were intravenous drug users, four of whom had at least one of the other risk factors listed above. Of the six cases (23.1%) who remained at NIR, 50% reported at least one episode of a sexually transmitted disease, 67% reported having sexual contact with prostitutes, 67% reported having been exposed to blood during sexual activity, and 100% reported recreational drug use. Among 74 controls, 11 (15%) reported CDC-defined behaviors associated with HIV infection. Four (5.5%) reported engaging in sexual activity with male partners, one (1.4%) reported intravenous drug use, and six (8.1%) had sex partners who used intravenous drugs.

Odds ratios and 95% confidence intervals were calculated for 11 potential risk factors. Results of the univariate analysis are presented in Table 1. The largest significantly elevated risk for HIV infection was found for male soldiers who, since 1980, engaged in sexual activity with male partners (OR = 22.9, 95% CI = 6.4–87.3). Only 1 case and 1 control

TABLE 1. Adjusted odds ratios for HIV infection according to behaviors reported since 1980

Behavior ^a	Cases	Controls	Odds ratio ^b	95% Confidence interval
Sexual activity with male partners	14	4	22.9	6.4-87.3
Anal sex	14	12	6.1	2.0-18.6
Sexual activity with a male or female partners which caused bleeding	14	6	14.9	4.6-49.2
Sexual activity with intravenous drug users	9	6	5.7	1.8-18.5
Sexual activity with more than two new partners per year	17	24	4.5	1.6-12.3
Group sex	14	14	6.8	2.3-19.7
Recreational drug use	24	55	3.2	1.1-9.4
Sexual activity with prostitutes	14	32	3.1	1.2-7.9
History of sexually transmitted diseases	14	29	1.8	0.7-4.9
Intravenous drug use	3	1	4.3	0.6-29.4
Oral sex	24	59	3.3	0.7-16.1

^a For each behavior, relative to a risk of 1.0 for men never engaging in that behavior.

^b Adjusted for age, length of military service, and race.

reported sexual activity exclusively with male partners, while 13 cases and 3 controls reported sexual activity with both male and female partners. Fourteen cases and 12 controls reported engaging in anal sex with either male or female partners, resulting in a significant OR of 6.1 (95% CI = 2.0-18.6). A significantly elevated risk of HIV infection was also found among soldiers who reported engaging in sexual activity that caused either himself or his male or female partner to bleed (exposure to menstrual blood was excluded) (OR = 14.9, 95% CI = 4.6-49.2). Eight cases and six controls reported blood exposure while engaging in sex with female partners (OR = 5.8, 95% CI = 1.7-19.9). Five cases and no controls reported blood exposure while engaging in sex with male partners and one case reported blood exposure during sex with both male and female partners. Other factors significantly associated with HIV infection included sexual activity with an intravenous drug user (OR = 5.7, 95% CI = 1.8-18.5), sexual activity with more than two new male or female partners per year since 1980 (OR = 4.5, 95% CI = 1.6-12.3), group sex (OR = 6.8, 95% CI = 2.3-19.7), recreational (nonintravenous) drug use (OR = 3.2, 95% CI = 1.1-9.4), and sexual activity with prostitutes (OR = 3.1, 95% CI = 1.2-7.9).

Table 2 presents the results of the multivariate unconditional logistic regression analysis. After adjustment for matching factors, any sexual activity with male partners, sexual activity which caused bleeding, sexual activity with intravenous drug users, and sexual activity with prostitutes remained independent risk factors for HIV infection.

DISCUSSION

The validity of HIV/AIDS risk factor data collected from military populations has been questioned (12-16), beginning with a widely publicized preliminary report of risk factors for HIV infection in active duty soldiers (4,17). The fact that the two most common modes of HIV transmission (sexual activity between men and intravenous drug use) are also grounds for discharge from military service has led many to feel that behavioral risk factor information collected from active duty men and women should be viewed with skepticism. Thus, a major component of our study design was to develop mechanisms to maintain the anonymity and confidentiality of our study subjects. The finding that 50% of the cases and 7% of the controls acknowl-

TABLE 2. Final logistic regression model for HIV infection among active duty male soldiers initially at no identified risk

Behavior ^a	Odds ratio ^b	95% Confidence interval	p
Sexual activity with male partners	21.9	4.5-107.8	0.0001
Sexual activity with male or female partners that cause bleeding	7.3	1.5-35.2	0.01
Sexual activity with prostitutes	3.8	1.0-14.4	0.05
Sexual activity with intravenous drug users	4.7	0.9-23.6	0.06

^a For each behavior, relative to a risk of 1.0 for men never engaging in that behavior.

^b Adjusted for age, length of military service, and race.

edged sexual activity with male partners or intravenous drug use, both of which may have jeopardized their military careers, suggests that many respondents felt that their anonymity was secure.

Based on a study design where the interviewer was blinded to the HIV-Ab status of the respondent, we found that 77% of cases initially at no identified risk of HIV infection and 15% of controls reported having at least one CDC-defined risk factor since 1980. Recently, the ongoing CDC NIR case series study has also reported reclassifying approximately 80% of AIDS cases initially reported as NIRs (18,19). In addition, the CDC study found that 46% of cases remaining at NIR reported having sexual contact with prostitutes, 33% reported a history of sexually transmitted diseases, and 22% reported recreational drug use (not including marijuana), which are behaviors also reported by the six remaining NIRs in our investigation.

In the final multiple logistic regression model, four behaviors were significant or marginally significant independent predictors of HIV infection—sexual activity with male partners, sexual activity with either male or female partners which caused bleeding, sexual activity with prostitutes, and sexual activity with intravenous drug users. Earlier epidemiological investigations have shown that homosexuals/bisexuals and individuals who had sex with intravenous drug users were at increased risk of HIV infection (20–25). Recent studies, however, suggest that men who were exposed to blood during sex with male partners were at particularly high risk of infection (26–28). Padian (29) has also proposed that blood exposure during sex is a risk factor for HIV infection among women. To our knowledge, the risk of HIV infection for men who are exposed to blood during vaginal sex or insertive anal sex with female partners has not been fully evaluated. Although numbers were small, based on the univariate analysis, it is of interest that we found a significant sixfold risk of HIV infection for men who reported exposure to blood during sex with female partners.

It is also noteworthy that we found a marginally significant risk of infection for men engaging in sexual contact with female prostitutes. While a previous case series report, based on HIV-infected soldiers, proposed that sexual contact with a female prostitute may be a risk factor for HIV infection (4), other studies with control groups have also reported an association between HIV infection and prostitute contact (30–33). Since reporting bias is a pos-

sible explanation for this finding in our study as well as in other studies (34), more data are needed to evaluate this risk behavior, particularly in Western cultures.

Several risk behaviors showed significant univariate associations with HIV infection, but did not remain in the final multiple logistic model. Of note, anal sex and group sex were associated with over a sixfold increase in risk of HIV infection. In addition, sexual activity with more than two new partners per year showed nearly a fivefold increase in risk. Both anal intercourse (particularly receptive anal intercourse) and the number of sexual partners have been found in other studies to be significant predictors of HIV-Ab status (24,28,35–39). In this study, the risk associated with receptive anal sex could not be determined since neither cases nor controls reported engaging exclusively in this behavior.

We also did not find any association in the univariate or multivariate analysis with self-reported history of sexually transmitted diseases. A history of gonorrhea and nonspecific urethritis were the two most commonly reported diseases; however, no meaningful differences were found based on case-control status. Four cases and no controls reported a prior history of syphilis.

Several factors need to be considered when interpreting the results of this investigation. First, despite our attempts to minimize misclassification, some respondents may have underreported certain risk behaviors and overreported others. In addition, the small sample size may have resulted not only in our inability to detect risk behaviors or sexually transmitted diseases known from other studies to be associated with HIV infection, but it also did not allow us to evaluate some factors in greater detail.

In summary, results of this pilot study, which was designed to maintain the confidentiality and anonymity of study subjects, suggest that it is possible to elicit reliable sexual behavior and drug use information from an Army population. The behaviors identified in this case-control study and in other studies of prevalent HIV infection, however, reflect determinants of risk associated with infections that occurred in the past. Future studies that involve newly infected, incident seroconverters will be extremely valuable in efforts to assess infection transmission dynamics as the epidemic evolves.

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